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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/881,509	06/24/1997	DOLORES J. SCHENDEL	P564-7015	3145

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EXAMINER
DECLOUX, AMY M

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/27/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
08/881,509	Schendel
Examiner	**Art Unit**
DeCloux, Amy	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Oct 10, 2001

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 2, 4-7, 26, and 45-47 is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 2, 4-7, 26, and 45-47 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 08/881,409 .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. The request filed 10/10/01 (Paper No. 27) for a continued Prosecution Application (CPA) under 37 CFR 1.53.(d) based on parent application No. 08/881,509 is acceptable and a CPA has been established. An action on the CPA follows.

2. Applicant's submission of a verified translation of the foreign priority document of Federal Republic of Germany Application No. 196 25 191.5 filed on 24.06.1996 is acknowledged. The previously stated 102 (a) rejectionhas been withdrawn. Because applicant has not addressed the outstanding 112 first and second paragraph rejections, they are maintained.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. MAINTAINED Claims 2, 4-7, 26 and 45 **and newly added claims 46-47** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid which codes for an alpha chain of the human T cell receptor comprising SEQ ID NO:23 where $X_1...X_n$ is one of the amino acid sequences recited in Part a) of Claim 2 of the instant application, a Fab, a single chain antibody, or soluble TCR fragments thereof , and a composition thereof, does not reasonably provide enablement for the broader recitation where $X_1...X_n$ are any amino acid sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation. Besides the nucleic acid that encodes for a human T cell receptor comprising SEQ ID NO:23, where $X_1...X_n$ is one of the amino acid sequences recited in Part a) of Claim 2 of the instant application, a Fab, a single chain antibody, or a soluble TCR fragment, or composition thereof, the specification fails to provide sufficient guidance in determining if either a nucleic acid that encodes any amino acids designated by $X_1...X_n$, or a nucleic acid that encodes a CDR region that is at least 80% identical to the amino acid sequence of SEQ ID NO:23, will encode an alpha chain of a T cell

receptor (TCR) with the desired specificity. Furthermore, while recombinant techniques are available, it is not routine in the art to screen large numbers of nucleic acids which code for a specific CDR3 where the expectation of retaining similar encoding function is unpredictable based on the instant disclosure. Detailed information regarding the structural and functional requirements of the CDR3 region of an alpha TCR specific for kidney carcinoma, as disclosed in the instant specification, other than the CDR3 sequences recited in Part a) of claim 2 of the instant application, is lacking. Also, recognition of a T cell epitope depends on the interaction of CDR3 with the MHC-peptide complex. Therefore, predicting that any nucleic acid that encodes any amino acids designated by $X_1...X_n$, that would maintain the desired specificity is well outside the realm of routine experimentation; thus a skilled artisan would require guidance, such as information regarding the sequence of derivatives and fragments which preserve the TCR specificity, in order to make and use polynucleotides, probes, vectors, host cells and recombinant methods in a manner reasonably commensurate with the scope of the claims. Thus, it would require undue experimentation of one skilled in the art to practice the claimed invention. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. **Note** that part (a) of claim 2 and newly added claim 46 encompass more 4mers or trimers than the nine recited in the instant claims because of the open language of the phrase "from the group comprising" in line 7 of claim 2 .

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

7. MAINTAINED Claims 2, 4-7, 26 and 45 **and newly added claims 46- 47** are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

In the instant case, the specification does not convey to the artisan that the applicant had possession, at the time of invention, of 1) a nucleic acid molecule which codes for an amino acid sequence with an equivalent recognition specificity, as achieved with a T cell receptor comprising a CDR3 region with the amino acid sequence of SEQ ID NO:23 for the peptide components of the T cell receptor ligands as recited in Part B)

of Claim 2 and dependent claims or 2) a nucleic acid that encodes a CDR region that is at least 80% identical to the amino aicd sequence of Part (a) as recited in claim 47. SEQ ID NO:23 which is YCLXXXXXSARQLTF encompasses 5 residues denoted by "x" which can be any amino acid. Percent identity language also denotes that any 1 or 2 of the defined amino acids of SEQ ID NO:23 can be replaced in any combination with any amino acid. Peptide components of the T cell receptor ligands can encompass any number of amino acid sequences. Due to this broad definition of a CDR3 sequence comprising SEQ ID NO:23 and the broad number of Peptide components of the T cell receptor ligands, none of these peptides (with the exception of the peptides recited in part A) of claim 2 and dependent claims) meets the written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See Vas-Cath, page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath, page 1116.). The skilled artisan cannot envision all the contemplated peptides that are components of the T cell receptor ligands, nor all peptides with an equivalent recognition specificity as achieved with a T cell receptor comprising a CDR3 region with the amino acid sequence of SEQ ID NO:23, or with 80% identity with the amino aicd sequence of Part (a) as recited in claim 47., and therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

Note that part (a) of claim 2 and newly added claim 46 encompass more 4mers and trimers than the nine recited in the instant claims because of the open language of the phrase "from the group comprising" in line 7 of claim 2 . Therefore, only the peptides which comprise the one of the nine 4mers or trimers recited in part A of Claim 2, but not the full breadth of the instant claims, meets the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

9. MAINTAINED Claims 2, 4-7, 26 and 45-47 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 4-7, 26 and 45 are indefinite for being in improper Markush format. The Office recommends the use of the phrase "selected from the group consisting of ..." with the use of the conjunction "and" rather than "or" in listing the species. See MPEP 2173.05(h).

B) Claim 2 and dependent claims 4-7, 26 and 45-47 are also indefinite for being in improper Markush format. It is noted that Claim 2 has two Markush groups.

The first commences at line 3 and lists members (a) and (b) in the rest of the body of the claim. This is improper because "selected from" must be followed by --the group consisting of--; also "or" at the end of Part (a) must be changed to --and--.

The second Markush group is nested within part(a) of the first Markush group. In line 4 of part (a) in claim 2, "comprising" must be changed to --consisting of--.

Part (a) of claim 2 is indefinite because it first defines X1...Xn as representing a sequence of 3-5 amino acids. The nine member Markush group recited un part (a) however, has only 3-mer and 4-mer sequences.

NEW GROUNDS OF OBJECTION AND REJECTION

10. Claim 26 is objected to for its recitation in line 1 of "contains as active" because it is awkward language. Inserting "an" before the word "active" would overcome this objection.

11. *35 U.S.C. § 101* reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

12. Claim 6 is rejected under 35 U.S.C. 101 because, the claimed invention is directed to non-statutory subject matter. A "cell", as recited in Claim 6 would read on a B lymphocyte cell in a subject and thus of an intact organism, which is a naturally-occurring product of nature and thus

constitutes non-statutory subject matter. Adding the phrase "an isolated" to the beginning of said claim would overcome his rejection.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy DeCloux whose telephone number is (703) 306-5821. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Amy DeCloux, Ph.D.
Patent Examiner
December 21, 2001

David A Saunders

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